Indications for house dust mite allergen–specific immunotherapy

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Introduction

Atopy is a genetic predisposition to the development of immunoglobulin E (IgE)–mediated hypersensitivity reactions to certain antigens or allergens.[1] The production of allergen-specific IgE seen in atopy is closely linked to clinical allergy and may manifest in a variety of ways, such as allergic rhinitis, asthma, atopic dermatitis, and food allergies. Allergic diseases can be precipitated by exposure to inhalable allergens, such as house dust mites (HDM), which are ubiquitous in indoor environments.

Local prevalence and disease burden

The prevalence of allergic diseases is 40% among school-aged children in Hong Kong.[2] *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* are the most commonly sensitised HDM allergens among local patients with allergic rhinitis and allergic asthma,[2-4] with a sensitisation rate of 81.9% among local children with physician-diagnosed asthma.[5] Conventional first-line treatments for allergic diseases include intranasal, topical, and oral medications for symptom control,[3] but patients may not achieve satisfactory disease control, especially if a treatment regimen requires daily compliance.[3] Chronic symptoms may also limit the self-image and psychosocial interactions of patients.[6] Allergy therefore carries significant disease burden, both at the individual and societal levels.

Characteristics of allergen-specific immunotherapy

Allergen-specific immunotherapy (AIT), which is yet to be popularised in Hong Kong, is a disease-modifying therapy.[3] It modifies the host immune system to the state of immunological tolerance by reducing mast cell activity and IgE release in response to allergen exposure, while also increasing numbers of regulatory T-cells.[3]

House dust mite allergen–specific immunotherapy

There are various AIT formulations, including those that target HDM allergens.[4] The initiation of HDM AIT requires that allergic disease be diagnosed by a physician and that sensitisation be demonstrated by measurement of serum HDM-specific IgE levels or a positive skin prick test to extracts from *D pteronyssinus* and *D farinae*. Following confirmation of sensitisation, the physician and patient agree on the route (subcutaneous immunotherapy [SCIT] or sublingual immunotherapy [SLIT]) and frequency of administration. The treatment begins with a build-up phase, which requires more frequent administration, daily for SLIT and weekly for SCIT, as the dose is increased to the maximally tolerable level. This is followed by the maintenance phase, which sustains allergic control.[4] Patients are monitored post-administration for any adverse effects (AEs) in a setting with emergency treatment kits; any significant AEs may warrant dose adjustment or even treatment cessation. The treatment may last from 1 to 3 years depending on the route of administration,[7] though its effect can be observed as early as 8 weeks following commencement.[8]

The indications for HDM AIT are discussed further below, including considerations around both disease factors and patient factors.

Disease factors

Severity

Clinical confirmation of allergic disease and atopy-triggered disease burden are equally important for assessing severity, with the latter categorised using established grading systems, including the ARIA (Allergic Rhinitis and its Impact on Asthma) guideline,[9] the Asthma Control Test,[10] and the Scoring Atopic Dermatitis (SCORAD) index.[11] Both the ARIA guideline and the Asthma Control Test assess the effects of allergic disease and atopic symptoms on quality of life and activities of

daily living; at the same time, they inquire about sleep disturbances and use of rescue medication, respectively.[9,10] On the other hand, the SCORAD index includes both subjective assessment of pruritus and sleep disturbance as well as objective signs of typical cutaneous manifestations.[11]

Contra-indications

Concomitant use of beta-blockers and poorly controlled asthma are well-established and absolute contra-indications to AIT,[12] since these patients are at risk of more severe AEs and treatment-resistant anaphylaxis.[7,12] In fact, the majority of AIT-associated deaths have occurred in severe asthmatics.[13]

Relative contra-indications include coexisting active autoimmune disease and active malignancies,[14] since there is an argument for the use of a risk-benefit analysis in such patients. Despite the theoretical risks of exacerbating the coexisting disease or reducing the effectiveness of AIT, there is limited real-world evidence regarding either outcome.[14] Pregnant patients are also advised against AIT initiation and dose up-titration[7,12] in view of the risks posed by anaphylaxis to the mother and the fetus.[7]

Patient factors

Acceptability

Patient selection for HDM AIT should adopt a personalised approach, with reference to its acceptability, affordability, cost-effectiveness, and, most importantly, patient preferences.[15] The two major forms of HDM AIT available in Hong Kong are SCIT and SLIT. Both can be administered in adults and children, despite limited data in those aged <5 years or >65 years.[7] For patients averse to repeated injections,[7] SLIT may be preferred.

Affordability

As a long-term treatment, the cost of AIT must be considered. While it is a self-financed item and mainly administered as a private healthcare service in Hong Kong,[15] the cost is covered by health insurance in some countries.[16] The availability of insurance coverage and ease of making claims are significant factors in patients continuing treatment.[16]

Cost-effectiveness

Although the costs of AIT are not available for public reference, several studies have assessed its incremental cost-effectiveness ratio.[7] Healthcare authorities in countries across the world set their own cost-effectiveness thresholds, albeit with varying values, and treatments with sub-threshold incremental cost-effectiveness ratios are considered to be cost-effective. Real-world studies have reported that AIT is cost-effective when assessed using quality-adjusted life years as a metric.[7,17]

Effectiveness

Patients may be hesitant about receiving treatment because it is not immediately effective. However, contrary to the popular belief that AIT takes years to work, clinical improvements can be observed at as early as 8 weeks for ocular symptoms (any watery, red, gritty or itchy eyes) and 14 weeks for nasal and asthmatic symptoms.[8,18] The onset of action varies according to treatment dose and the type and severity of allergic disease.[8]

Allergen-specific immunotherapy, which is currently the only curative therapy for allergy, is associated with long-term symptom remission.[19] In a study by Cools et al,[19] patients with asthma either received the standard level of care or HDM AIT. Those in the intervention group experienced milder and less frequent asthmatic symptoms, and these improvements persisted throughout the mean follow-up period of 9.3 years after completion of AIT.

Immunotherapy may also reduce the development of new allergies. For example, administration of HDM AIT to paediatric patients with allergic rhinoconjunctivitis was found to be an effective primary prevention strategy against progression to asthma, according to Jacobsen et al.[20]

Safety profile

The AEs of AIT may be of concern to some. Local AEs are common and include injection site redness, swelling, and pain for SCIT, and sublingual and throat itchiness for SLIT. Systemic AEs are more common for patients treated with SCIT.[3,7] Though rare, anaphylaxis is potentially life-threatening, but can be readily managed using patient-administered intramuscular adrenaline injections. Patients receiving SCIT require monitoring for AEs for 30 minutes prior to discharge. The likelihood of AIT-associated AEs may be reduced by coadministration of anti-IgE injections.[7]

Immunotherapy in polysensitised patients

In cases of allergen polysensitisation, the physician may be uncertain regarding whether to initiate single- or multi-allergen immunotherapy; unfortunately, there is no definitive answer in this situation. The efficacy and safety profiles of multi-allergen AIT have not been established, making this novel approach unvalidated.[21] However, patients may be emphatic about their wish for complete symptom eradication and aggressive desensitisation to all allergens.

Local allergists typically adopt the European approach by choosing one major allergen for which there are commercially available extracts; physicians using the North American approach may opt for extracts produced in-house that allow for tailored, multi-allergen immunotherapy.[21] Ultimately, treatment is often based on the patient's preference

and their frequency of exposure to each allergen, especially for pet dander. The unknown anaphylactic risk with multi-allergen immunotherapy may be overcome by close and extended monitoring post-administration, such as for a few hours, at a facility with available resuscitation support.

Treatment adherence

Like conventional oral and inhaled corticosteroids, SLIT requires daily administration,[7] potentially leading to noncompliance. In paediatric patients undergoing SLIT, family support and supervision are critical, as SLIT is usually administered daily by a trained family member.

Conclusion

Allergen-specific immunotherapy is an evolving field. By reviewing the most up-to-date information available, this commentary has endeavoured to facilitate better doctor-patient communication for those undergoing and prescribing HDM AIT, with the aim of achieving optimal allergic control to improve the physical and psychosocial health of these patients.

Author contributions

Concept or design: All authors.
Acquisition of data: CWM Leung, HC Chu, JCH Leung.
Analysis or interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: TF Leung.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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References

1. Hill DA, Spergel JM. The atopic march: critical evidence and clinical relevance. Ann Allergy Asthma Immunol 2018;120:131-7.
2. Wong GW, Li ST, Hui DS, et al. Individual allergens as risk factors for asthma and bronchial hyperresponsiveness in Chinese children. Eur Respir J 2002;19:288-93.
3. Chan AW, Luk WP, Fung LH, Lee TH. The effectiveness of sublingual immunotherapy for house dust mite-induced allergic rhinitis and its co-morbid conditions. Immunotherapy 2019;11:1387-97.
4. Nelson MR, Cox L. Allergen immunotherapy extract preparation manual. Available from: https://www.aaaai.org/Aaaai/media/Media-Library-PDFs/Practice%20Management/Practice%20Tools/Ch-9-Allergen-Immunotherapy-Extract-Preparation-Manual-correction-July-19-12.pdf. Accessed 18 Jan 2023.
5. Leung TF, Li AM, Ha G. Allergen sensitisation in asthmatic children: consecutive case series. Hong Kong Med J 2000;6:355-60.
6. Chida Y, Hamer M, Steptoe A. A bidirectional relationship between psychosocial factors and atopic disorders: a systematic review and meta-analysis. Psychosom Med 2008;70:102-16.
7. Roberts G, Pfaar O, Akdis CA, et al. EAACI Guidelines on Allergen Immunotherapy: allergy rhinoconjunctivitis. Allergy 2018;73:765-98.
8. Nolte H, Maloney J, Nelson HS, et al. Onset and dose-related efficacy of house dust mite sublingual immunotherapy tablets in an environmental exposure chamber. J Allergy Clin Immunol 2015;135:1494-501.e6.
9. Demoly P, Calderon MA, Casale T, et al. Assessment of disease control in allergic rhinitis. Clin Transl Allergy 2013;3:7.
10. American Thoracic Society. Sleep related questionnaires. Available from: https://www.thoracic.org/members/assemblies/assemblies/srn/questionaires/act.php. Accessed 18 Jan 2023.
11. Severity scoring of atopic dermatitis: the SCORAD index. Consensus report of the European Task Force on Atopic Dermatitis. Dermatology 1993;186:23-31.
12. Moote W, Kim H, Ellis AK. Allergen-specific immunotherapy. Allergy Asthma Clin Immunol 2018;14(Suppl 2):53.
13. Bernstein DI, Wanner M, Borish L, et al. Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990-2001. J Allergy Clin Immunol 2004;113:1129-36.
14. Pitsios C, Demoly P, Bilò MB, et al. Clinical contraindications to allergen immunotherapy: an EAACI position paper. Allergy 2015;70:897-909.
15. Chan YT, Ho HK, Lai CK, et al. Allergy in Hong Kong: an unmet need in service provision and training. Hong Kong Med J 2015;21:52-60.
16. Vaswani R, Liu YC, Parikh L, Vaswani S. Inadequate health insurance coverage: a major factor in premature discontinuation of subcutaneous immunotherapy for allergic rhinitis. Ear Nose Throat J 2011;90:170-3.
17. Farraia M, Paciência I, Castro Mendes F, et al. Cost-effectiveness analysis of house dust mite allergen immunotherapy in children with allergic asthma. Allergy 2022;77:2688-98.
18. Wang DH, Chen L, Cheng L, et al. Fast onset of action of sublingual immunotherapy in house dust mite-induced allergic rhinitis: a multicenter, randomized, double-blind, placebo-controlled trial. Laryngoscope 2013;123:1334-40.
19. Cools M, Van Bever HP, Weyler JJ, Stevens WJ. Long-term effects of specific immunotherapy, administered during childhood, in asthmatic patients allergic to either house-dust mite or to both house-dust mite and grass pollen. Allergy 2000;55:69-73.
20. Jacobsen L, Niggemann B, Dreborg S, et al. Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study. Allergy 2007;62:943-8.
21. Calderón M, Cardona V, Demoly P; EAACI 100 Years of Immunotherapy Experts Panel. One hundred years of allergen immunotherapy European Academy of Allergy and Clinical Immunology celebration: review of unanswered questions. Allergy 2012;67:462-76.